PATENT SPECIFICATION

DRAWINGS ATTACHED

899,807

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International Classification:—A61m. B65d. B67b.

COMPLETE SPECIFICATION

A method of Dispensing a Free-Flowing Comminuted Solid and an article therefor

We, THE WELLCOME FOUNDATION LIMITED, a British Company of 183-193 Euston Road, London, N.W.1 do hereby declare the invention for which we pray that a patent may be granted to us and the method by which it is to be performed to be particularly described in and by the following statement:—

The present invention relates to a method of dispensing a free-flowing comminuted solid and an article therefor.

Certain substances used in relatively dilute solutions cannot be stored as such because the potency of such solutions falls with time. It has been a formidable problem to prepare, on the spot, sterile solutions of these substances at the dilution required, for example, for injectable solutions of drugs, or for culture media for microorganisms or tissue cells. In this specification, a vitamin is included within the meaning of the word drug.

Succinyl choline, a short-acting muscle-relaxant drug frequently administered intravenously to the patient during a surgical operation, is unstable as an injection solution but is more stable in concentrated solution. It has been proposed to prepare its sterile injectable solutions from sterile components by the following procedure. The drug is provided in concentrated solution in a container with a hypodermic needle which punctures the diaphragm in the closure of a container of diluent packed under reduced pressure. The drug is thus automatically sucked into the bottle of diluent thereby preparing an injectable solution. This method is not entirely satisfactory since the drug must still be stored in solution, and the success of the mixing operation depends on the preservation of a vacuum in the diluent container.

The present invention in one aspect provides a method of aseptically transferring a free-flowing comminuted solid into a container of diluent from an internally sterile collapsible container which is partially filled with the free-flowing comminuted solid with a gas-filled space above it and has an outlet normally closed by a gas-pressure-responsive device, which method comprises opening a channel of communication between the outlet of the collapsible container and the container of diluent, causing the gas pressure inside the collapsible container to exceed that exterior to the outlet so that the gas-pressure-responsive device is pneumatically displaced outwards, and allowing the free-flowing comminuted solid to flow from the collapsible container into the container of diluent.

A drug can thus be transferred with certainty and under sterile conditions into a container of diluent to form an injectable solution. The diluents commonly employed for injectable solutions of drugs are isotonic saline solutions which may contain small quantities of glucose.

The present invention in another aspect provides an article for storing a free-flowing comminuted solid and dispensing it into a container of diluent, which comprises an internally sterile collapsible container bearing a dispensing member exterior to and communicating with the outlet of the container, in which the collapsible container is partially filled with a free-flowing comminuted solid with a gas-filled space above it, the outlet of the collapsible container is normally closed by a stopper adapted to be pneumatically displaced into the dispensing member on causing the gas pressure inside the collapsible container to exceed that in the dispensing member, and the dispensing member contains a tilting device for tilting the stopper after displacement to permit unrestricted flow of the free-flowing comminuted solid through the dispensing member.

The accompanying drawings show specific embodiments illustrating the invention.

Figure 1 is an elevation of a collapsible container; that is, a container which is deformable with an accompanying decrease in

[*Price*

its internal volume.

Figuer 2 is a vertical section of an article comprising a collapsible container, a dispensing member, and a valve seat with a form of valve as a gas-pressure-responsive device closing the outlet of the collapsible container, and having means in position for aseptically covering the dispensing member before use.

Figure 3 is a vertical section of the article of Figure 2 in use in the preparation of a sterile solution.

Figure 4 is a plan view of the seat of Figures 2 and 3.

Figure 5 is a vertical section of a valve seat with another form of valve.

Figure 6 is a plan view of the seat of Figure 5.

Figure 7 is a vertical section of a form of stopper assembly as the gas-pressure-responsive device closing the outlet of the collapsible container.

Figure 8 is a plan view of the assembly of Figure 7 with the stopper in position.

Figure 9 is a partial vertical section of an article having the stopper assembly of Figure 7 in use in the preparation of a sterile solution.

Figure 10 is a vertical section of the article comprising a collapsible container, a dispensing member and another form of stopper assembly closing the outlet of the collapsible container, and having means in position for aseptically covering the dispensing member before use.

Figure 11 is a vertical section of the article of Figure 10 in use in the preparation of a sterile solution.

Figure 12 is a horizontal section of the article of Figure 10 in use illustrating the relationship of the displaced stopper and the interior of the dispensing member.

Figure 13 is a vertical section of the stopper assembly of the Figure 10 without the stopper.

As shown in Figure 1, a collapsible container 10 of flexible polyethylene or similar synthetic plastic material has a mouth at the end of an externally threaded neck 11 at the base of which is an integral knurled flange 12 for the retention of a seal to be hereinafter described.

As shown in Figure 2, the collapsible container 10 is partially filled with a free-flowing comminuted solid with an air space above it. The neck 11 of the collapsible container 10 receives an elastic seat 13 of rubber or synthetic plastic material having a depending annular skirt portion 14. The upper portion of the seat 13 is in the form of a disc of greater diameter than the skirt portion to provide a supporting ledge for the seat when positioned in the neck 11. In the embodiment illustrated in Figures 2, 3 and 4, a flap valve 15 is formed in the upper disc portion of the seat 13 and can open and close in either direction under the influence of a change of gas pressure in the body portion of the collapsible container 10. An internally threaded dispensing member 16 incorporating a channelled piercing device is threaded on to the neck 11 of the collapsible container 10 in such a manner that the outer flange of the upper portion of the seat 13 is clamped between an annular shoulder formed internally above the threaded portion of the dispensing member and the lip of the container mouth. Before the article is used, a protective sheath 17 of synthetic plastic material is normally positioned over the dispensing member 16. When the parts are assembled as shown in Figure 2, an annular flexible seal 18 of synthetic plastic material is shrunk or otherwise suitably applied over the portion of the assembly including a knurled flange 19 on the lower part of the protective sheath 17, a knurled flange 20 on the dispensing member 16 and the knurled flange 12 on the neck 11 of the collapsible container 10. The knurled flanges prevent relative movement of the assembled parts under the seal.

As shown in Figure 3, the flexible seal 18 and protective sheath 17 are removed before use thereby exposing the dispensing member 16 incorporating the channelled piercing device. The collapsible container 10 is then inverted and a frangible diaphragm 21 of a container 22 of diluent is punctured by the piercing device on the dispensing member 16 which then projects into a passage 23 within the neck of the container of diluent. The application of pressure to the walls of the collapsible container 10 forces open the flap valve 15 and causes the comminuted solid to flow from the collapsible container through the open valve and the dispensing member 16 into the solution in the container 22 of diluent.

Figures 5 and 6 show another form of gas-pressure- responsive device. A seat 24 has a skirt portion 25 and is formed with a plurality of radial slits 26 which come together at a central point of the upper disc portion of the seat.

Figures 7 and 8 illustrate a stopper assembly comprising a seat 27 of rubber or synthetic plastic material having a depending annular skirt portion 28 which is received in the neck 11 of the collapsible container 10. A stopper 29 is normally frictionally held in an opening in the seat. Figure 9 illustrates the operation of an article having the stopper assembly shown in Figures 7 and 8 wherein the stopper 29 has been blown out of the seat 27 by pressure applied to the collapsible container 10. In this embodiment, the dispensing member 16 is formed with a number of inwardly directed fins 30 to prevent the loose stopper 29 from occluding the passage.

In Figures 10 and 11 is shown an article having another form of stopper assembly.

The elastic seat 31 of rubber or synthetic plastic material has a skirt portion 32 which is received in the neck 11 of the collapsible container 10. A stopper 33 is frictionally held in an opening in the seat 31. The sides of the opening in the seat 31 are oblique as illustrated in Figures 10, 11 and 13 in order to prevent accidental displacement of the stopper 33. As is shown in Figures 10, 11 and 12 the dispensing member 16 is formed with an integral inwardly directed fin 34. The intentional application of pressure to the walls of the collapsible container 10 forces the stopper 33 out of the seat 31. The stopper 33 comes to rest eventually at a slanted position on the internal fin 34 inside the dispensing member 16. The comminuted solid then flows freely from the collapsible container 10 through the opening in the seat 31, past the displaced stopper 33 and through the dispensing member 16 into the solution in the container 22 of diluent. The fin 34 is an improved form of fin as it tilts the displaced stopper 33 and prevents it from becoming centered and occluding the passage.

WHAT WE CLAIM IS:—

1. A method of aseptically transferring a free-flowing comminuted solid into a container of diluent from an internally sterile collapsible container which is partially filled with the free-flowing comminuted solid with a gas-filled space above it and has an outlet normally closed by a gas-pressure-responsive device, which method comprises opening a channel of communication between the outlet of the collapsible container and the container of diluent, causing the gas pressure inside the collapsible container to exceed that exterior to the outlet so that the gas-pressure-responsive device is pneumatically displaced outwards, and allowing the free-flowing comminuted solid to flow from the collapsible container into the container of diluent.

2. A method claimed in Claim 1, in which the channel of communication between the outlet of the collapsible container and the container of diluent is opened by means of a channelled piercing device borne on and communicating with the outlet of the collapsible container.

3. An article for storing a free-flowing comminuted solid and dispensing it into a container of diluent, which comprises an internally sterile collapsible container bearing a dispensing member exterior to and communicating with the outlet of the container, in which the collapsible container is partially filled with a free-flowing comminuted solid with a gas-filled space above it, the outlet of the collapsible container is normally closed by a stopper adapted to be pneumatically displaced into the dispensing member on causing the gas pressure inside the collapsible container to exceed that in the dispensing member, and the dispensing member contains a tilting device for tilting the stopper after displacement to permit unrestricted flow of the free-flowing comminuted solid through the dispensing member.

4. An article claimed in Claim 3, in which the dispensing member incorporates a channelled piercing device for opening a channel communication between the outlet of the collapsible container and the container of diluent.

5. An article claimed in Claim 3 or Claim 4, in which the tilting device is a fin projecting from the inside of the dispensing member.

6. A method of aseptically transferring a free-flowing comminuted solid into a container of diluent from an internally sterile collapsible container which is partially filled with the free-flowing comminuted solid with a gas-filled space above it and has an outlet normally closed by a gas-pressure-responsive device, substantially as herein described with reference to Figures 1, 2, 3 and 4 of the drawings.

7. A method of aseptically transferring a free-flowing comminuted solid into a container of diluent from an internally sterile collapsible container which is partially filled with the free-flowing comminuted solid with a gas-filled space above it and has an outlet normally closed by a gas-pressure-responsive device, substantially as herein described with reference to Figures 5 and 6 of the drawings.

8. A method of aseptically transferring a free-flowing comminuted solid into a container of diluent from an internally sterile collapsible container which is partially filled with the free-flowing comminuted solid with a gas-filled space above it and has an outlet normally closed by a gas-pressure-responsive device, substantially as herein described with reference to Figures 7, 8 and 9 of the drawings.

9. A method of aseptically transferring a free-flowing comminuted solid into a container of diluent from an internally sterile collapsible container which is partially filled with the free-flowing comminuted solid with a gas-filled space above it and has an outlet normally closed by a gas-pressure-responsive device, substantially as herein described with reference to Figures 10, 11, 12 and 13 of the drawings.

10 An article for storing a free-flowing comminuted solid and dispensing it into a container of diluent, substantially as shown in Figures 1, 2, 3 and 4 of the drawings and herein described with reference thereto.

11. An article for storing a free-flowing comminuted solid and dispensing it into a container of diluent, substantially as shown in Figures 5 and 6 of the drawings and herein described with reference thereto.

12. An article for storing a free-flowing comminuted solid and dispensing it into a

container of diluent, substantially as shown in Figures 7, 8 and 9 of the drawings and herein described with reference thereto.

13. An article for storing a free-flowing comminuted solid and dispensing it into a container of diluent, substantially as shown in Figures 10, 11, 12 and 13 of the drawings and herein described with reference thereto.

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Chartered Patent Agent.

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899807 COMPLETE SPECIFICATION

3 SHEETS *This drawing is a reproduction of the Original on a reduced scale*

Sheet 1

Fig.1

Fig.2

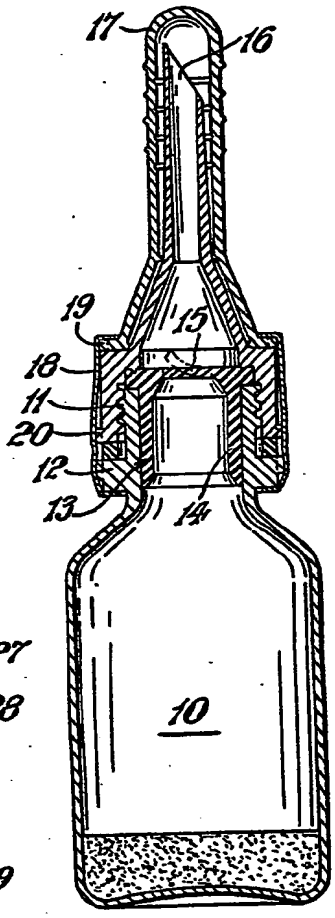


Fig.5

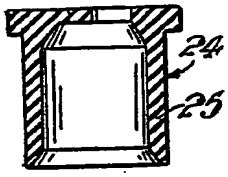


Fig.7

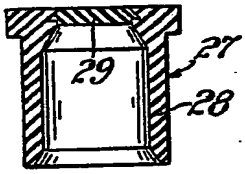


Fig.6

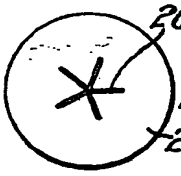
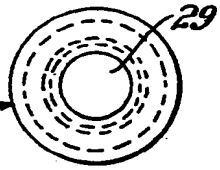


Fig.8



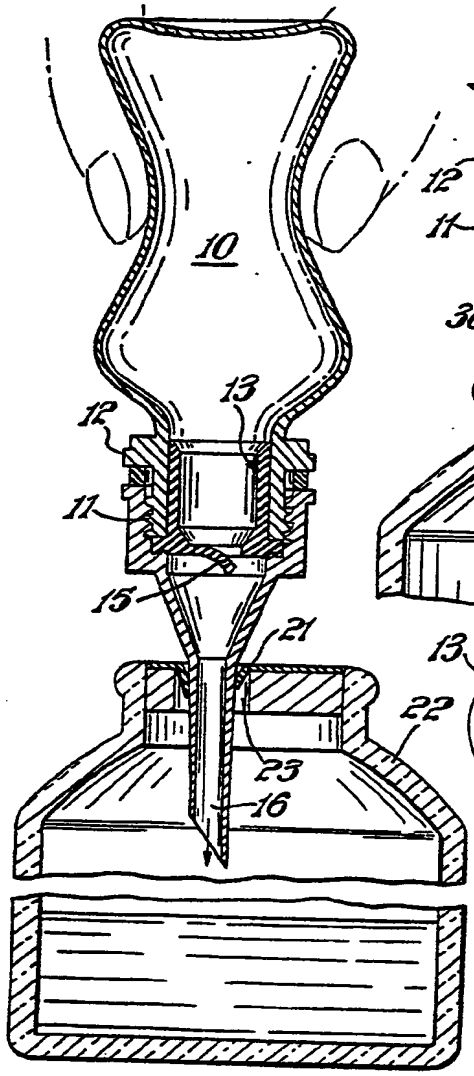


Fig.3

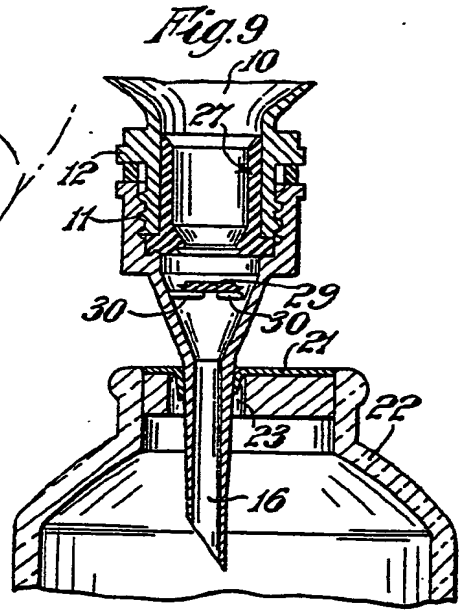


Fig.9

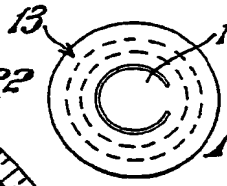


Fig.4

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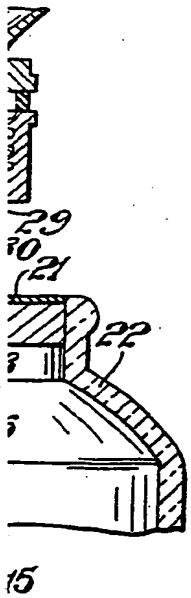

Fig. 4

Fig. 10

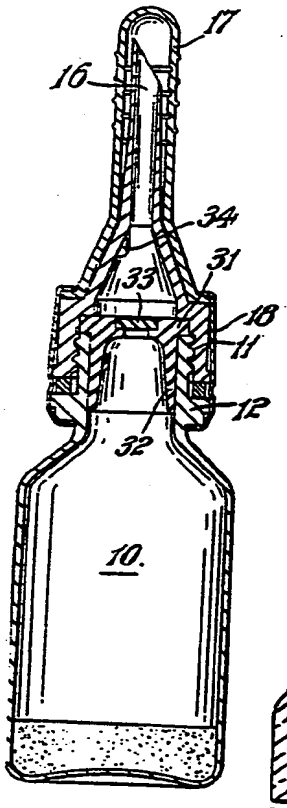

Fig. 11

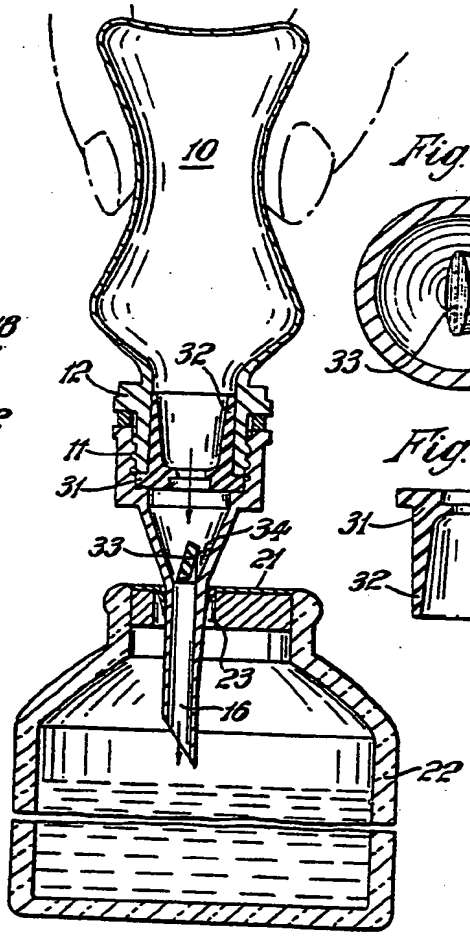

Fig. 12

Fig. 13

899807 COMPLETE SPECIFICATION
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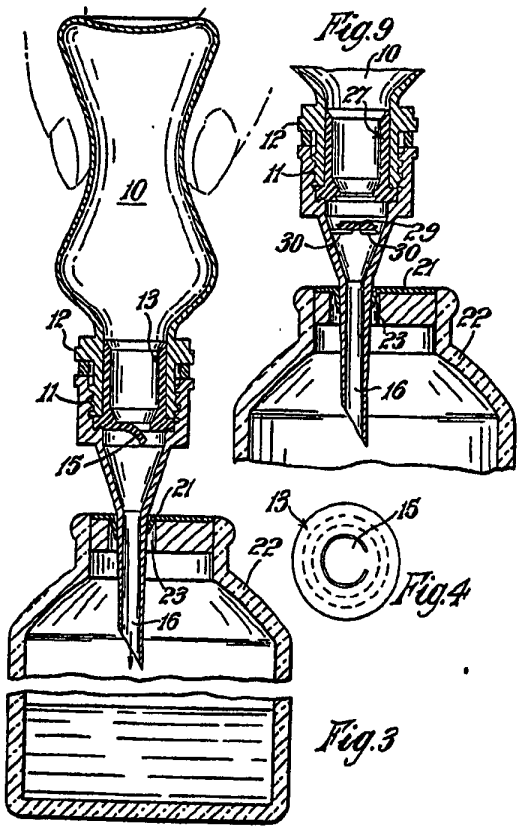

Fig.3

Fig.9

Fig.4

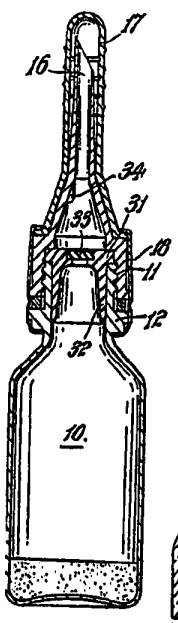

Fig.10

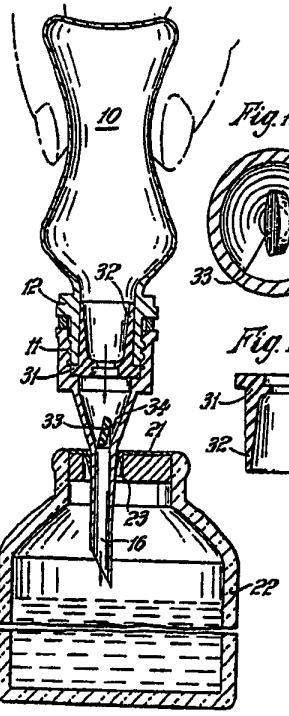

Fig.11

Fig.12

Fig.13